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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/015,499	12/11/2001	Kevin P. Baker	GNE.2830P1C42	6886

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 09/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/015,499	BAKER ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/15/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *4x references*.

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement filed 10/15/02 fails to comply with 37 CFR 1.98(a)(2), which requires all other information or that portion which caused it to be listed. It is noted that the Blast results cited therein are not true publications with a publication date, and therefore, are not fully in compliance with 37 CFR 1.97. Thus, they will not be printed on the face of the patent issuing from this application. It is further unclear what, if any, publication, the Blast results are intended to represent. They have been placed in the application file, but the current information referred to therein cannot be fully considered, as it relates to whether the Blast results indicate prior art, for those references crossed out.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 C(1).

Specification

2. The specification should be reviewed for improper recitation of hyperlinks. All such recitations should be deleted or amended such that the hyperlinks are rendered inactive. See MPEP § 608.01.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 28-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

The claims are directed to isolated polypeptides corresponding to SEQ ID NO: 397, and referred in the specification as PRO1788. The specification discloses that PRO1788 is a "*novel* polypeptide having homology to leucine-repeat proteins", in which "protein containing leucine-rich repeats are thought to be involved in protein-protein interactions", and that "it is presently believed that PRO1788... is a *newly identified* member of the leucine-rich repeat-containing family and may possess activity or properties typical of the leucine-rich repeat-containing family"[emphasis added] (pgs. 33, 264 & 353). Page 32 then states that "[p]rotein-protein interactions include receptor and antigen complexes and signaling mechanisms". However, the instant specification does not disclose any additional information regarding PRO1788, as to whether it is a receptor or antigen complex or merely involved in an undefined signaling mechanism. Although page 353 does disclose that PRO1788 has "*certain* amino acid sequence identity with... 'GARP Human' [emphasis added]", the function of 'GARP Human' is unknown in the art at the time of filing Applicants' invention, and also is not described within the instant specification.

The sole assay disclosed within the specification is that PRO1788 tested positive in the gene amplification assay (Example 143, pgs. 494-503 & 506). This information may provide a

credible, specific and substantial utility for PRO1788 nucleic acids, but not for PRO1788 polypeptides or antibodies. In other words, the preliminary data in the specification were not supported by analysis of mRNA or protein expression. Accordingly, the literature reports that it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased polypeptide expression, such that the claimed polypeptides would be useful for diagnosis of cancer or as a drug target. For example, Pennica et al. (1998) disclose that:

> "An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient." (see page 14722, 2nd pp).

Likewise, Konopka (1986) state that:

> "Protein expression is not related to amplification of the abl gene but to variation in the level of bcr-abl mRNA produced from a single Ph1 template" (see abstract).

In arguendo, even if gene amplification did correlate with increased transcription in a particular situation, it does not always follow that protein levels are also amplified. For example, Haynes et al. (1998) studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript level. For some genes, equivalent mRNA levels translated into protein abundances that varied more than 50-fold. Haynes therefore concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (pg. 1863, 2nd paragraph, and Figure 1). Thus, the art

indicates that it is not the norm that gene amplification, or even increased transcription, results in increased protein levels.

Overall, it is unknown what specific physiological significance PRO1788 plays (e.g., pg. 256). Therefore, one cannot reasonably extrapolate what constitutes a specific utility for the polypeptide of SEQ ID NO: 397, because the *specific* "qualitative biological activity" for the polypeptide depicted as SEQ ID NO: 397 is not known in the art for this "novel polypeptide", nor specifically described within the specification (e.g., pg. 266). Although the specification does generally assert a utility that all of the disclosed PRO polypeptides may be useful in isolating other polypeptides to which they bind, used as molecular weight markers, used in tissue typing, used in therapy, or used to identify agonists or antagonists, virtually any polypeptide generically possesses these putative uses. However, none of these asserted utilities are *specific* to the claimed PRO1788 polypeptide. Moreover, in that no activity has been specifically assigned to PRO1788, any assay requiring PRO1788 to discover putative binding partners, or agonists/antagonists, cannot reasonably be conducted until the specific biological activity of PRO1788 is determined empirically. Thus, no "specific" utility reasonably exists for this "novel polypeptide " of SEQ ID NO: 397.

Second, these asserted utilities are further not "substantial", because significant further experimentation is necessary at the time of filing the instant invention to attribute a "real world" utility for the polypeptide SEQ ID NO: 397. For example, the specification provides no nexus between any specific disease state and a correlative change in the amount or form of PRO1788 at the time of filing Applicants' invention. In fact, the specification has assigned no specific activity to PRO1788. Therefore, the skilled artisan is prevented from extrapolating what assays

need to be developed to search for other molecules associated with PRO1788, or what disease states may be amendable to treatment through administration of the PRO1788 polypeptide. Thus, the instant invention also has no "substantial utility". See MPEP 2107.

In summary, because the proposed use of the PRO1788 polypeptides are simply starting points for further research and investigation into potential practical uses of the polypeptides, the instant claims have no specific nor substantial utility, consistent with that held by the court in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966):

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

5. Claims 28-33, 36-37 & 39-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes on page 299 that "the amino acid sequence (SEQ ID NO: 397) [was] derived from the [putative] coding sequence of SEQ ID NO: 397 shown in Figure 231". Pages 264 & 353 of the specification disclose that PRO1788 is a "*novel* polypeptide having homology to leucine-repeat proteins", and that PRO1788 has "*certain* amino acid sequence identity with... 'GARP Human' [emphasis added]". However, the function of 'GARP Human' is unknown in the art, and also not described within the instant specification. The sole written description is the single *human* polypeptide species described is PRO1788 of SEQ ID NO: 397. No written description is provided in the specification for any other species of PRO1788 molecules, nor for any variants thereof (i.e., including molecules "having at least 80%, 85%, 90%, 95% or 99% amino acid sequence identity to SEQ ID NO: 397, polypeptides "comprising" "extracellular domains of the polypeptide", or chimeric polypeptides thereof). Nor is any written description provided in the specification for what distinguishable function characteristics these other generic polypeptides would possess, since none are known or described. In other words, the claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature. Therefore, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. To provide evidence of possession of a claimed genus, the specification must

provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Here, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is no identification of any particular portion of the structure that must be conserved. Thus, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus because one skilled in the art can not structurally visualized any functional amino acid sequence, except for the single disclosed human sequence of SEQ ID NO: 397; thereby, not reasonably meeting the written description requirements of 35 U.S.C. 112, first paragraph. See MPEP 2163.

Accordingly, *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, *as of the filing date sought*, he or she was in possession *of the claimed invention*". "The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed* [emphasis added]".

6. Claims 28-33, 36-37 & 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The polypeptide identified as PRO1788 is disclosed to possess two transmembrane domains in Figure 232, which would result in multiple extracellular domains. Therefore, it is unclear what is meant by the recitation of "extracellular domain" in the current claims.

Moreover, if the polypeptide possesses an extracellular domain, the recitation of "the extracellular domain...lacking its associated signal sequence" is indefinite (e.g., claims 28(d) & 37), because a signal sequence is not generally considered to be part of an extracellular domain, in that signal sequences are cleaved from such domains during secretion from the cell.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 28-33, 36-37 & 39 are rejected under 35 U.S.C. 102(a) as being anticipated by Koehrer et al. (clone DKFZp586E011; Protein Sequence Database Accession No. T14791; August 1999).

Koehrer et al disclose a human polypeptide that is 99.6 % identical to residue #s 112-353 of SEQ ID NO: 397, which comprises the extracellular domain between residue # 305-353 of PRO 1788 and/or comprises 100% sequence identity of the extracellular domain between residue # 233-286 of PRO 1788, which further lacks the associated signal peptide of residue #s 1-16 (i.e., as it relates to claims 28©&(d), 29©&(d), 30©&(d), 31©&(d), 32©&(d), 33©&(d), 36 & 37), and which comprises heterologous amino acid residues when compared to the putative extracellular regions of SEQ ID NO: 397 (i.e., as it relates to claim 39).

It is noted that the above rejection is based in part upon a disclosure provided in a computer database record. Because the database was indexed so as to be available to the relevant part of the public, it is considered to be a U.S.C. § 102; see *In re Wyer*, 210 USPQ 790.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961. The fax phone number for this Group is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert C. Hayes, Ph.D.
September 10, 2004

ROBERT C. HAYES, PH.D.
PATENT EXAMINER